ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

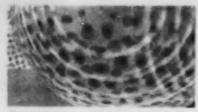
esearch news

THE

PUZZLE

ARE WE SOLVING IT?

On the Cover



Steven Courbe is an Edmorton arise who is stoovering from ricit and throat cancer. The cover art, entitled "I Feel Safe" is part of a series of paintings. Courbe completed throughout the process of his diagnosis and treatment.

AHFMR Mission

AHFMR supports a community of researchers who generate knowledge whose application improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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research news

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SPRING 2005

Breathing problems in babies

Dr. John Greer wants to know why some babies can't breathe properly.

The cancer puzzle

Alberta-based researchers continue to add to the growing body of knowledge on cancer, adding piece by piece to the cancer puzzle.

(f) InnerVision

Calgary-based InnerVision Medical Technologies Inc. has developed a tool for early detection of breast and prostate cancer.

The source of seigures

Life can be very difficult for people whose epilepsy can't be controlled with prescription drugs. Dr. Paolo Federico wants to help.

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The AHFMR Newsletter is published four times annually and in distributed free of charge to a controlled circulation fint within Canada. If you wish to receive it, places contact us by phore, e-real, fee or by letter. It is also on the self-at worsubfercab.co.

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Contents copyright of AHTHIR.
ISSN 1703-6694 (online)
Cabadian Publications Agreement \$40054910



Perhaps more than any other health problem, mental illness engages the legal system. How these interactions affect the treatment of persons with mental illness is a subject of keen interest to the Rt. Hon. Beverley McLachlin, Chief Justice of Canada. She makes a strong case for law and medicine to work together to ensure that society does not overlook the needs and the rights of mentally ill persons.

e are at the beginning of a vital and fascinating chapter in the saga of legal medicineone that engages the major philosophical concerns of the law," says Chief Justice McLachlin. "One cannot go very deeply into mental health issues without encountering the big questions: When is it just to hold a person responsible for criminal acts? Can the law limit the right to refuse hospitalization and medical treatment, and if so, where do the limits lie? What rights do family and society have to impose treatment? And what obligation do we, the healthy, owe to our less fortunate

Attitudes toward the mentally ill have improved as advances in

brothers and sisters?"

medicine have yielded greater understanding of diseases of the mind. As well, the law has changed greatly in recent years in how it treats mentally ill offenders. Nonetheless, mental illness still poses problems in both criminal and civil law. (Criminal law deals with infractions against the Criminal Code and other federal legislation.

Civil law covers disputes between individuals, such as when a mentally ill person is forced to receive treatment.)

In Canadian crimi-

nal law, there is no longer such a thing as a defence on the grounds of insanity; rather, a person may be found "not criminally responsible on account of mental disorder" today. "This signifies that we are

from the community

"Law and medicine need to join hands and move together"

no longer faced
with a stark
choice
between
acquittal and
conviction of
mentally ill
persons,"
explains Chief

Justice McLachlin. "The law now offers a third alternative, under which mentally ill offenders are diverted into a special stream where the twin goals of protecting the public and treating the ill offender fairly and appropriately are pursued." Unfortunately, a lack of adequate treatment resources can hamper rehabilitation under this regime.

Mental illness poses different problems in the civil justice system. The issues here tend to involve personal autonomy and access to treatment.

Today, all Canadian jurisdictions permit the involuntary hospitalization of people who present a danger to themselves or others. Laws dealing with these matters vary from province to province-according to whether the particular jurisdiction adopts a "dangerousness" or a "treatment" model of civil commitment. In some provinces, the perceived danger must be of physical or bodily harm. In others, a broader notion of danger is used, and the risk of serious mental, emotional, social, or even financial harm may justify forced hospitalization. Still others have gone beyond dangerousness to allow involuntary hospital admission with a view to preventing substantial mental or physical deterioration. There is

Voices

no clear answer here, and the competing values of autonomy, treatment, and protection continue to play out in Canadian courtrooms.

The legal and ethical issues raised by these problems are very difficult and complex. Chief Justice McLachlin notes that the problems are far from being solved, and expects that we will continue to grapple with them for the foreseeable future. But she is not daunted, and suggests a way forward—one that involves lawyers and doctors working together.

"To proceed in isolation, to get out of step with each other, will result in less-thaneffective solutions," she says. "Law and medicine need to join hands and move together in this area. Laws cannot

heal people; only service

and treatment provided by medical professionals can do that. But the law can create a social and regulatory environment

that assists medical professionals in delivering their services in a manner that is both ethical and respectful of the rights and needs of the mentally ill."

Chief Justice McLachlin gave the lecture "Medicine and Law: The Challenges of Mental Illness" at the University of Alberta and the University of Calgary in the framework of the 2005 Honourable Mr. Justice Michael O'Byrne/AHFMR Lecture on Law, Medicine and Ethics.



AHFMR frequently receives letters requesting information about Heritage research or about various medical conditions.

"Responding to the Reader" is an AHFMR
Research News feature intended to provide up-to-date information related to
readers' questions, with the help of
experts in the Alberta research community.

AHFMR cannot provide medical advice, however; please see your family physician about your specific health concerns.

> What research is being conducted on the complications of spinal cord injury?

while loss of movement is one of the most obvious consequences of spinal cord injury, many other serious complications are major health issues for people with spinal cord injury. Such secondary conditions as loss of bladder and bowel control, pressure sores, and spasticity dramatically affect quality of life.

Researchers at the University of Alberta are responding to the need for better treatment of these conditions. Heritage Scientist Dr. Arthur Prochazka and Hentage Scholar Dr. Vivian Mushahwar are known for their expertise in functional electrical stimulationapplying electrical currents to generate activity in the nervous system. In particular, they are using a new procedure called intraspinal microstimulation (ISMS), which involves implanting hair-like microelectrodes into a very specific region of the spinal cord to stimulate mus-

cle contractions. Much

of their work aims to

induce controlled limb movements similar to normal walking, but they are also applying the technique to other complications. For example, Dr. Prochazka leads a team that is investigating the potential application of ISMS to improve bladder control, and Dr. Mushahwar has recently turned her attention to pressure sores.

Pressure sores develop in wheelchair-bound and bed-ridden individuals. Most of these ulcers are caused by skin breakdown due to continuous surface abrasion, moisture, and low hygiene, but some occur because of localized and sustained external pressure when deep muscle tissue dies. This latter type of pressure sore is the most dangerous; difficult to detect, it causes severe damage and there is currently no effective strategy to prevent it. Dr. Mushahwar has submitted a grant proposal to develop an electrical stimulation method that would prevent the formation of pressure sores in individuals with spinal cord injury.

Both Dr. Mushahwar and Dr. Prochazka emphasize that their work focuses on exploring the potential of ISMS.

Such conditions dramatically affect quality of life Developing this knowledge into effective treatments for spinal cord injury is a long-term undertaking.

In related research, Heritage Senior Scholar Dr. David Bennett studies the extreme is a long-term muscle spasms that plague many people with spinal cord injury. These exaggerated reflexes occur because some of the neurons (individual nerve cells) in the lower spinal cord become more sensitive after injury. However, because of the injury, the brain can no longer send signals to regulate the contractions. Medication can control spasticity, but the drugs work systemically and dampen all nerve impulses not a desired outcome for a person with a spinal cord injury. Dr. Bennett's research is aimed at understanding how neurons become hyperexcitable. This is fundamental work that is years away from application in humans. @

Dr. Arthur Prochazka is a Heritage Scientist, and a full professor in the Department of Physiology in the Faculty of Medicine and Dentistry at the University of Alberta. He also receives funding from the Canadian Institutes of Health Research (CIHR) and the US National Institutes of Health (NIH)

Dr Vivian Mushahwar is a Heritage Scholar, and an assistant professor in the Department of Biomedical Engineering in the Faculty of Medicine and Dentistry She also receives funding from CIHR, NIH, and the Canada Foundation for Innovation (CFI)

Dr. David Bennett is a Heritage Senior Scholar, and an associate professor in the Division of Neuroscience, part of the Faculty of Rehabilitation Medicine at the University of Alberta. He also receives funding from CIHR, the CFL and NIH Breathing problems BABIES Whether it involves studying respiratory muscles or brain-stem cells controlling breathing, Heritage Scientist Dr. John Greer's research has one theme: understanding why some babies can't breathe properly.



The diaphragm: an essential muscle for breathing

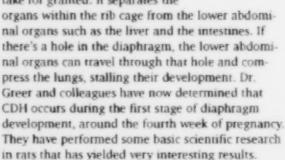
"My interest is in understanding the basis for breathing problems in babies; all of my research centres around that theme," explains Dr. Greer, a University of Alberta physiology professor. "I study one muscle

Babies with CDH develop holes in their diaphragms in particular that plays a central role in breathing: the diaphragm. Some of my research focuses on a devastating condition called congenital diaphragmatic hernia or CDH, which many people have never even

heard of. Essentially, babies with CDH develop holes in their diaphragms while still in the womb. These babies have lungs that don't properly develop, and they often die in their first few days of life. We are now beginning to scratch the surface of what's really going on with CDH."

CDH occurs in one out of every 2,500 births, an incidence similar to that of cystic fibrosis. Dr. Greer is intent on finding out what occurs during development to cause this condition. The diaphragm is a

sheet of muscle that contracts and relaxes to help expand and contract the rib cage, forcing air in and out of the lungs during breathing. It also has a second function, which many people take for granted: it separates the



"If we expose pregnant female rats to a chemical called nitrofen, we find their offspring develop the exact same holes in their diaphragms as the human fetus," explains Dr. Greer. "We've studied each part of development in the rat, and what we've discovered is that nitrofen perturbs the vitamin A pathway. Pregnant female rats fed a diet deficient in vitamin A, again, have offspring with the same holes. We're now using animal models, with genes controlled by the vitamin A pathway knocked out, to further our understanding of the cause of CDH."

Dr. Greer stresses that the lack of vitamin A in fetuses that develop CDH likely has nothing to do with how much vitamin A mothers have in their diets. "It's not that mothers aren't getting enough vitamin A, it's that these babies can't unlize or access it. There may be a problem with transfer from mother to fetus. These infants may have a genetic defect which causes the holes; that's something we still have to find out. Expectant mothers should not be taking high doses of vitamin A because it does not prevent CDH and too much can cause birth defects."

Currently, there is no way to prevent CDH. "Of course our long-term goal is to prevent it," says Dr. Greer, "but we're still at the stage of trying to understand what's going on." Dr. Greer and University of Alberta neonatologists Dr. Bernard Thébaud (a Heritage Clinical Investigator) and Dr. Thierry Lacaze are establishing a multi-centre study examining vitamin A levels in babies born in Alberta, Ontario, Quebec, and the Netherlands.

The developing brain and breathing

Another area of research in Dr. Greer's lab is neural control of infant breathing. Along with Heritage Senior Scholar Dr. Gregory Funk and Heritage Scientist Dr. Klaus Ballanyi, Dr. Greer studies the brain stem, where breathing is controlled. This internationally recognized research group is interested in how this part of the brain develops and how it functions before birth and immediately following birth.

"This area of the brain can shut off after a child goes to sleep, causing the child to stop breathing for fifteen to twenty seconds," says Dr. Greer, noting that when this happens in an adult, we know it as sleep apnea. "During sleep, a set of nerve cells in the brain stem may not be excited enough, or their activity may actually be depressed, and breathing ceases. The airway may even collapse, because when these nerve cells are on, they release neuro-transmitters to keep the airway open. These repeated bouts of lack of oxygen are of concern for the proper development of babies."

The difficulty in studying how nerve cells in the brain control breathing lies in the fact that the brain stem has many different types of nerve cells mingling with one another, each responsible for different functions in the body. As few as 700 nerve cells may be responsible for breathing, a small number of the total

nerve cells in the brain stem. The challenge was to separate the nerve cells responsible for breathing from the rest. Silvia Pagliardini, an AHFMR-funded Ph.D. student in Dr. Greer's laboratory, took advan-

tage of the fact that the nerve cells responsible for breathing have a receptor on their surface called substance P, which is not found on any other type of cell in the brain stem. She then used a special tag that recognizes substance P and binds to it. When viewed under a fluorescent microscope, the

tag glows and those cells with substance P light up and can be isolated.

Dr. Greer is excited about this new methodology. "This is a substantial development for researchers who study breathing and development. Now that we can visualize and isolate these cells, it will completely change the way we study problems like apnea and devise ways to stimulate breathing with drugs."

A rewarding career

Dr. Greer became involved in research in his teens, participating in summer research programs. He's been hooked ever since. "I immediately took a liking to research and have never had any doubts that working at a university and participating in medical research is the ideal profession for me. One of the greatest pleasures in this line of work is interacting with young trainees. I believe that much of my labo-

ratory's success over the past twelve years is the result of exceptional students and postdoctoral fellows. Although the laboratory has made fundamental advances toward understanding what is necessary for newborns to breathe properly, I feel that the best is yet to come."

AHFMR Scientist Dr. John Greer is an associate professor in the Department of Physiology in the Centre for Neuroscience at the University of Alberta. Dr. Greer's work is also supported by the Canadian Institutes of Health Research (CIHR), the March of Dimes, and the Alberta Lung Association.

Selected publications

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Healthy sch



If you have children or adolescents at home, you'll know how tough it is to give them all the right messages. You want to warn them about the risks of drugs, alcohol, smoking, unprotected sex, and an unhealthy diet...and sometimes you wonder if they're listening.

A University of Calgary researcher and her colleagues are working with parents, teachers, and others to reach young people where they spend most of their day: in school. The education system already recognizes that schools are an ideal setting for prevention and health-promotion activities; now health psychologist Dr. Laura Ghali is investigating whether strengthening the social environment in schools can also help teens change their behaviour. Dr. Ghali believes that a school's social setting can be an important contributor to adolescent health, well-being, and learning. She suggests that if you can enhance the social environment, you will achieve multiple benefits for students, teachers, support staff, and the community.

Dr. Ghali works with Heritage Senior Scholar Dr. Penny Hawe at the University of Calgary's International Collaborative Centre for the Study of Social and Physical Environments and Health, funded by the Canadian Institutes of Health Research (CIHR). The Centre's goal is to improve understanding of how everyday settings—such as schools, neighbourhoods, and workplaces—influence health. Dr. Ghali designs and evaluates programs in Alberta schools that she hopes will improve outcomes for students and increase work satisfaction for teachers and staff.

Dr. Ghali suggests that although a school's function is to teach students to read, write, and compute, it also serves another purpose. It's important that kids feel they belong at school, that they feel connected to their teachers and peers. Studies show that kids who are highly engaged in school and feel that it is a welcoming place, have more positive academic and health outcomes. For instance, students who dislike school are more likely to fail academically, and are at greatest risk of adopting unhealthy behaviours, exhibiting problems due to mental

ools, healthy choices

stress, and experiencing reduced quality of life.
"Students need various supports in place," explains
Dr. Ghali. "They can receive support from their family, from their school, or from a spiritual connection
in their lives. All of these appear to be protective
when it comes to health-risk behaviours. We also
know that teachers make a huge difference in students' lives and to their ability to be engaged in
school and engaged in learning."

While schools are ideal settings for health promotion, they are also settings in which health can worsen, points out Dr. Ghali. "If students are alienated

from school—perhaps they feel isolated or they're being bullied—then their health can actually deteriorate in that setting. Our interest is in trying to improve the social environment in schools so that all students feel they belong and have a meaningful role to play." A recent study showed that students who are being "bullied" at school are more likely to drink, smoke, use marijuana, and report symptoms of depression.

Schools often try to address students' health problems by organizing health-promotion activities that tackle individual risk behaviours one at a time. For instance, one year a high school may focus on bullying. At. ther year, the school may try to address smoking or binge-drinking. Dr. Ghali and her colleagues advocate an approach that is very different from this piecemeal strategy: they look at the whole school. Their strategy considers not only the curriculum offered in the classroom, but also how the classroom functions as a social setting in which students need to feel safe, connected, and valued. Other factors are also important how the school operates as a social institution, for example; how inviting it is to families, and how inclusive; and how it collaborates with community organizations-and



that kids feel connected to their teachers and peers

can ultimately have an impact on the students' health and well-being.

All schools have a health curriculum but, Dr. Ghali points out, there's not a lot of evidence that these information-based programs actually work.

Many school health-promotion programs are ineffective in bringing about behavioural change. Some may even cause harm. The International Collaborative Centre aims to help Alberta's health regions and schools choose programs wisely. "We need more time and resources devoted to evaluating what works," says Dr. Ghali. "I don't believe the onus to do that is on schools. I think we, as health researchers, need to provide schools with an array of choices that are evidence-based, so they can be confident that programs they provide are safe and effective."

It's also important to understand the school context and how it interacts with a program, she adds. "You might have a fabulous program that works in



"We need to provide schools with an array of choices"

one school beautifully, but in another school it becomes a disaster." The key is for the curriculum to focus on social connection and mental health promo-

tion as a foundation for good health behaviours, such as engaging in physical activity and choosing a healthy diet, and deciding not to drink, smoke, use drugs, or have unprotected intercourse.

"Life is a series of challenges, particularly for adolescents who are facing a lot of stresses and are dealing with some decisions for the first time," says Dr. Ghali. "What's really becoming clearer for me is that to actually make healthy choices, you need to have a foundation of good mental health, selfesteem, and social support."

Dr. Ghali and her colleagues are currently involved in a pilot project with Brooks Composite High School. The intervention is designed to improve the social environments and health of rural teens and attempts to expand on the findings of a successful Australian study. Now in its third year, the project involves collaboration between the University of Calgary, the University of Lethbridge, the Palliser Health Authority, and the Centre for Adolescent Health in Melbourne, Australia. The next step is to add four Calgary Board of Education schools to the project. The researchers at the International Collaborative Centre also hope to extend this research over the next few years, including a large-scale intervention study in as many as 40 Alberta schools, beginning in 2006.

Dr. Laura Ghali works at the International Collaborative Centre for the Study of Social and Physical Environments and Health at the University of Calgary and is a research associate in the Department of Community Health Sciences. She receives support from the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness. She also receives funding from the Canadian Institutes of Health Research, Alberta Alcohol and Drug Abuse Commission (AADAC), and Health Canada.

For Dr. Marie Fraser,
the story of what
keeps us alive is all
in the details.

e study enzymes," says Dr. Fraser, an AHFMR Medical Scholar. "Without enzymes, we'd be non-existent."

An enzyme is a large molecule whose job is to speed up a chemical reaction in a living cell. "The reactions that take place in our body would normally take place too slowly for a biological system," Dr. Fraser explains, "so you need the enzymes to speed up these reactions." An enzyme in our stomach called pepsin, for example, helps us digest food by breaking large protein molecules into smaller protein components called peptides.

Dr. Fraser focuses on two enzymes that perform vital tasks in different ways: succinyl-CoA synthetase (SCS) and CoA transferase. Knowing exactly how each enzyme works would help drug designers ensure that new medications don't interfere with the enzymes' life-sustain-

Dr. Fraser focuses on two enzymes succinyl-called heme, which goes



"The reactions that take place in our body would normally take place too slowly for a biological system, so you need the enzymes to speed up these reactions."

into the oxygen-carrying hemoglobin in red blood cells. SCS also helps us metabolize energy. "It really speeds things up, performing its job thousands of times per second," Dr. Fraser says.

In 1994, Dr. Fraser and her research team were the first in the world to describe the structure of SCS. "And we're still trying to figure out how it works," she says with a laugh. SCS performs its very complicated reaction by binding to three separate smaller molecules or substrates. Dr. Fraser's team has learned that this binding takes place in two different locations on the larger SCS molecule. "What connects the two is that there's actually a part of the enzyme that moves."

The other enzyme, CoA transferase, speeds up a reaction that turns compounds called ketone bodies into energy. Ketones are produced in the liver and released into the bloodstream whenever the level of glucose (sugar) in people's blood drops, such as during fasting or starvation. Some people are born

with a genetic mutation in CoA transferase that prevents the enzyme from doing its job, and in rare cases, individuals have died because the ketones then poisoned the cells in their

Ketones are produced in the liver

body; however, people with the condition can stay healthy simply by eating carefully.

Crystallography is the key technique Dr.

Fraser and her team use to study the structure of both enzymes. The technique involves growing crystals of purified enzymes, similar to diamonds or crystals of salt in a salt shaker. Team members then place these crystals in a powerful X-ray beam, using a synchrotron at the University of California in Berkeley. A synchrotron is an incredibly intense light source the size of a football field. The machine produces a diffraction pattern from the crystals. From this pattern, Dr. Fraser and her team can use computers to reconstruct a detailed, atom-by-atom image of the enzyme's structure.

Dr. Marie Fraser is a Heritage Medical Scholar and an associate professor in the Department of Biological Sciences at the University of Calgary She also receives funding from the Natural Sciences and Engineering Council of Canada (NSERC) and the Canadian Institutes of Health Research (CIHR).

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THE CONTRACTOR PUZZLE

In all of us. According to the National Cancer Institute of Canada, approximately 38% of Canadian women and 43% of men will develop cancer in the course of their lifetimes.

About 1 in 4 Canadians will die of the disease.

Although the numbers are staggering,

they are partly due to population growth and aging, not to increased individual risk of cancer. And in the past two decades, researchers have made tremendous advances in various areas of fundamental research, advances that are increasingly being applied in the clinic in the form of new cancer treatments. With support from AHFMR, many Albertabased researchers continue to add to the growing body of knowledge-adding piece by plece to the cancer puzzle.

Reprogramming cancer cells

ne of those researchers is AHFMR Scholar Dr. Michael Hendzel, His work at the University of Alberta involves epigenetics-the study of changes in the activity of the gene that occur without a change in its DNA structure (the molecules that carry genetic information and pass changes on from one generation to the next). Researchers recently demonstrated that a cancer cell nucleus could be reprogrammed; in other words, the event that led to the onset of cancer could be undone while all the cell's DNA changes that preceded the onset remain intact. "That tells you there is an epigenetic component to cancer," explains Dr. Hendzel. "This is good news

"Epigenetic changes can be reversed"

because, unlike changes in DNA sequence, epigenetic changes can be reversed."

It's now estimated that at least as many changes in gene expression occur through epigenetic processes as through mutations in the DNA; deactivation of cancer tumour suppressors is a case in point. In the past, cancer researchers have focused on changes in the DNA sequence. Epigenetic changes hold new potential because of their reversibility. "If we had a full understanding of how epigenetic processes work, in theory we could reprogram the genome to behave the way we want," says

Dr. Hendzel, Along with two University of Alberta colleagues, experimental oncologist Dr. Gordon Chan and Heritage researcher and medical geneticist Dr. Alan Underhill. Dr. Hendzel studies a particular epigenetic modification that may facilitate rapid cell evolution-a major concern in cancer, where cells divide and grow very

quickly. Dr. Hendzel points out that the first generation of drugs targeting epigenetic processes is now coming to the clinic: non-toxic drugs that have great potential as chemotherapy. "There is real hope that these drugs can directly target cancer cell growth without having adverse effects on other processes," says Dr. Hendzel. "They have great potential for both treatment and prevention of cancers."

New tools

otential is also a word that drives the work of Heritage Scholar Dr. David Schriemer-the potential to use new tools in the study of cancer. An analytical chemist at the University of Calgary, Dr. Schriemer applies the tools of his field to cancer research. More specifically, he uses mass

spectrometry to study the structure and function of proteins (the workhorses of a cell). A mass spectrometer is an instrument used to measure the mass of molecules. "Think of it as a very sensitive bathroom scale for really. really small things," says Dr. Schriemer. He explains that there may be proteins in a cancerous sample that do not appear in normal tissue. Learning how these proteins interact with one another and what sort of problems in interaction lead to dysfunction could provide insight into how to better treat disease. "We want to see how a healthy person and a diseased person look on a molecular level," he explains. "Our tools are

Microtubules are an important target for cancer drugs

designed to quantify that difference."

One of Dr. Schriemer's projects involves the analysis of microtubules, hollow tubes in every cell system that play a role

in cell division. Since cancer cells divide at a faster rate than other cells, microtubules are an important target for cancer drugs aiming to slow down their cell division function—drugs such as Taxol (Paclitaxel), which is mainly used to treat breast and ovarian cancer tumours. Microtubules are very complex structures and relatively little is known about them. "If we can study their structure and function, maybe we can come up with a better drug to target microtubules," says Dr. Schriemer, "one with fewer side effects and better outcomes."

Diagnosis in the palm of your hand

hile Dr. Schriemer conducts his work on the basic end of the research spectrum, Dr. Linda Pilarski's research bridges the gap between the lab and the clinical setting. A

University of Alberta researcher working at the Cross Cancer Institute, Dr. Pilarski studies multiple myeloma. a particularly deadly type of cancer which affects plasma cells in the bone marrow. Part of her research looks at the early-stage cells that lead to this type of cancer. "These cells don't go away with any current type of cancer therapy," she explains. "Treatments such as chemotherapy target only the later-stage cells, which do not appear able to regenerate themselves. We also have to get rid of the early-stage cells that maintain the disease process, or the cancer will keep coming back." Dr. Pilarski has

these genes.

Her second line of investigation focuses on technology that could one day be applied in the clinic to help diag-

The device could revolutionize cancer diagnostic testing

nose cancer patients. As leader of the Alberta Cancer Diagnostic Consortium, Dr. Pilarski collaborates with engineer Dr. Chris Backhouse and medical geneticists and Heritage researchers Dr. Moira Glerum and Dr. Susan Andrew to develop a handheld diagnostic device—"a lab on a chip"—to analyze these early-stage cancer cells. The device could revolutionize cancer diagnostic testing, which is

identified two genes which help these early-stage

cells survive and is now testing a treatment to target



ABOVE: DR. DAVID SCHRIEMER RIGHT: DR. LINDA PILARSKI



currently timeconsuming and expensive, and requires specific expertise, whereas almost anyone could use the lab-on-a-chip. It could also be used

in many other fields of study. Dr. Pilarski was recently invited to Washington, DC, to give a symposium to members of the FBI on use of the technology for genetic testing in forensics.

The lab-on-a-chip project is supported through the Alberta Cancer Diagnostic Consortium, a unique collaboration between the universities of Alberta and Calgary and the Alberta Cancer Board, funded by Western Economic Diversification Canada, CIHR, NSERC and other agencies. This support has allowed scientists from a variety of backgrounds to work together in the same lab-an absolutely critical factor, according to Dr. Pilarski. "Things are going really well right now," she says of the project. "Having biomedical and engineering staff working in close proximity allows us to work more effectively, to make the device more efficient."

Life after treatment

r. Jana Rieger focuses on how patients cope following cancer treatment. For the approximately 400 people diagnosed with head or neck cancer in Alberta each year, even treatment considered successful can mean a serious reduction in their quality of life.

Patients who undergo radiation treatment often experience dry mouth due to the destruction of their salivary glands. The condi-

Head and neck cancer treatment can seriously reduce patients' quality of life

Waiting for treatment

How long should patients have to wait for breast cancer treatment? It's a question Alberta Health and Wellness research officer Edrick Androws hopes to answer through AHFMR's program called SEARCH (Swift Efficient Application of Research in Community Health).



ndrews points out that addressing the issue of wait-lists for care is one way of putting the customer first in healthcare—a major recommendation of the 2002 Premier's Advisory Council on Health report. Since treatment for breast cancer is one of the health system's pressure points, he hopes to find evidence to support an appropriate standard for waiting times.

In 2004, an estimated 1850 Alberta women developed breast cancer; 410 of them will most likely die of the disease.

"What would be an appropriate wait time to improve the outcome?" asks Andrews. "Among women diagnosed with breast cancer, what is the effect on survival of waiting for care? That is my research question."

To find the answer, he has been examining existing literature concerning wait times and their impact on survival. Phase 2 of his project. will involve studying Alberta-specific data from the Alberta Cancer Board and comparing it to the literature. "Based on these two things, we can use the evidence to support a standard for waiting time instead of simply relying on clinicians' experience, which is how standards are often

developed." @

Edrick Andrews is a research officer in the Quality and Accountability branch of Alberta Health and Wellness. SEARCH is an innovative program that trains people in health organizations to do and use health research. After eight years of success, AHFMR continues to fund this unique program in partnership with Alberta's health regions and the University of Calgary. through the jointly governed, not-for-profit corporation, SEARCH Canada, which is sustaining and extending the SEARCH program within and beyond Alberta

tion sounds minor, but it can have devastating effects. Without saliva, patients can develop cavities in their teeth and sores in their mouths; eating and speaking can become very difficult; and wearing dentures or other prostheses in the mouth may be problematic. Patients who speak for a living, such as teachers, might lose their jobs because they can no longer communicate very well. And society often judges them very harshly. A recent study found that people listening to recordings of the voices of patients who had undergone surgery for oral cancer tended to rate the speakers as less intelligent, less attractive, and less employable than average.

"A lot of people don't realize that when the capacity for either speech or eating has been taken away, the consequences are far-reaching," says Dr. Rieger, a Heritage Population Health Investigator and speech pathologist at the University of Alberta. "These people tend not to socialize with their friends or eat dinner with their families. They can feel very isolated and often become reclusive."

Dr. Rieger wants to help. She studies two different types of treatments to prevent dry mouth: a surgical treatment to transfer one of the salivary glands before radiation, and a drug treatment patients receive while undergoing radiation. To understand whether one method works better than the other, Dr. Rieger collects information about the patients'





speech, chewing and swallowing, and general quality of life before and after the treatments. She works with a unique multidisciplinary team of surgeons, oncologists, speech therapists, and prosthodontists (specially trained dentists who make replacements for missing teeth or other

structures in the mouth) at Edmonton's COMPRU facility—the Craniofacial Osseointegration and Maxillofacial Prosthetic Rehabilitation Unit—an internationally recognized centre of excellence for head and neck reconstruction. Here Dr. Rieger's work allows her to assess patients so that surgeons can change their tactics when something is not working well.

"We want to plan surgeries better, not just in terms of curing the cancer, but also for optimal function and quality of life for the patient," she says.

Colon cancer screening

eritage Population Health Investigator Dr.
Robert Hilsden focuses on screening patients
early to prevent them from developing colon
cancer. The third most common type of cancer in

Canada, colon cancer may also be the least talked about; many people are embarrassed to discuss

Colon cancer can be cured if caught early

symptoms which include changes in bowel movements. Colon cancer develops from polyps or tumours in the large intestine, which are harmless

LEFT: DR. JANA RIEGER

ABOVE: DR. POBERT HILSDEN

at first and develop into cancer only if not removed. Without early detection, about 45% of people diagnosed with

colon cancer die; but it can be cured if caught early. This is where Dr. Hilsden hopes to make a difference.

Colon cancer testing has received greater attention recently, partly because of the involvement of former hockey great Daryl

Sittler as a spokesperson to raise awareness of the disease. In addition, a colon cancer task force recently established guidelines suggesting that screening should begin at age 50.

"The real problem is: how do you put that into action?" says Dr. Hilsden, a University of Calgary researcher as well as a practising gastroenterologist. "Which test should be used, and how should it be implemented? There are also questions about cost. We want to understand the factors that influence people's decision-making in choosing a particular type of test; things like effectiveness, invasiveness, and whether or not they have to travel to have it done."

One of his research projects, in collaboration with AHFMR researchers Dr. Elizabeth McGregor and Dr. Gillian Currie, is an economic analysis of the various types of colon cancer tests. Dr. Hilsden also wants to determine the complication rate for colonoscopy, a test which uses a tiny camera to examine the inside of the large intestine.

A third project involves the fecal occult blood test—how often it is used, and whether people receive appropriate follow-up afterwards.

"This cancer is treatable," emphasizes Dr. Hilsden, "but we need to figure out the best way to catch it in its early stages."

Brain cancer

that is deadly but treatable, AHFMR
Clinical Investigator Dr. Ian Parney is
preoccupied with a type that has a much poorer
prognosis: brain cancer. A brain surgeon as well as a
researcher at the University of Calgary, Dr. Parney
studies glioblastomas—the most malignant type of
brain tumour. What causes these tumours is still a
mystery for the most part, but the end results are all
too well known. Average survival time for a patient
with this type of tumour is only about a year to 16
months; without treatment that time drops to 3 to 4
months. And despite advances in radiation

and chemotherapy, those survival rates have not improved a great deal over

the past 30 years.

Unlike other types of cancer, brain tumours seldom spread to other parts of the body; but they tend to return after surgery, in spite of the long hours surgeons like Dr. Parney spend removing them. "We need to learn more about how the immune system interacts with these tumours," he states. "We want to learn how to

Dr. Parney has been concentrating on trying to stimulate white blood cells called lymphocytes and macrophages to fight the tumours. While there are few lymphocytes in the tumours, macrophages are found in abundance. They act as housekeeping cells, chewing up debris such as tumours. Yet these

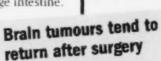
system to fight back."

stimulate the immune

macrophages seem to be subverted by the tumour to do its own dirty work—they may even be killing the lymphocytes. "My research is focused on how we can change this.

How can we turn those macrophages on so they attack the turnour?"

After several years in San Francisco, Dr. Parney returned recently to his hometown of Calgary, drawn



by AHFMR funding as well as by Alberta's strong research environment. "Heritage has been a big part of my research training," he says, pointing out that his career began with an AHFMR Summer Studentship, "And there has been such phenomenal growth in neuroscience. neuro-oncology, and neurosurgery here that we have one of the best, if not the best, groups of

THE

Diversification Canada: the CIHR New Emerging Teams (NET) Program, and NSERC.

Dr. Jana Rieger is an AHFMR
Population Health
Investigator and an
assistant professor
in the University of
Alberta Department
of Speech Pathology
and Audiology,
part of the Faculty
of Rehabilitation
Medicine.

Dr. Robert Hilsden is an AHFMR Population Health Investigator and an assistant professor in the University of Calgary departments of Medicine and Community Health Sciences. He also receives funding from the National

(Medical Services Incorporated) Foundation, and Calgary Laboratory Services.

Cancer Institute of Canada, CIHR, the MSI

Dr. Ian Parney is an AHFMR Clinical Investigator and an assistant professor in the departments of Clinical Neurosciences and Oncology at the University of Calgary

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Dr. Michael Hendzel, an AHFMR

people to work with in

place to be."

the world. Alberta is the

Scholar, is an associate professor in the University of Alberta Department of Oncology He receives funding from the Canadian Institutes of Health Research (CIHR), the Alberta Cancer Board, and the Alberta Cancer Foundation.

Dr. David Schriemer is an AHFMR Scholar and an assistant professor in the University of Calgary departments of Biochemistry and Molecular Biology; Oncology; and



Pharmacology and Therapeutics, and an adjunct assistant professor in the Department of Chemistry. He is the Canada Research Chair in Pharmaceutical Proteomics and receives funding from the CFL CIHR. Alberta Ingenuity (AHFMR's sister foundation for science and engineering research), and MDS Sciex. He is the director of the Southern Alberta Mass

Spectrometry Centre for Proteomics and a principal investigator of the Alberta Ingenuity Centre for Carbohydrate Science.

Dr. Linda Pilarski is a professor in the University of Alberta Department of Oncology and holds the Canada Research Chair in Biomedical Nanotechnology. She also receives funding from the US National Institutes of Health (NIH), CIHR, the Natural Sciences and Engineering Research Council of Canada (NSERC), the Alberta Cancer Board, and the National Cancer Institute of Canada. The lab-on-a-chip project receives support through the Alberta Cancer Diagnostic Consortium, funded by Western Economic

InnerVision



Breast cancer is the most frequently diagnosed cancer in Canadian women. On average, 100 women die of breast cancer every week. X-ray mammography is the current screening convention for breast examination, but it has some significant limitations. The discomfort of breast compression is a barrier to some patients, and the imaging of dense breasts and small breasts has yielded poor results. Among Canadian men, prostate cancer is the most frequently diagnosed cancer. The disease is significantly underdetected. There is currently no imaging technology available for effective screening of prostate cancer, and an average of 81 men die of it in Canada every week.

Plank Miredward offers early detection for breast and proctate cursor InnerVision's technology, called Flash UltraSound, offers a non-invasive means of early detection for breast, prostate, and other types of cancer. It combines innovative acoustic wave analysis

with the computational power of supercomputing, providing superior image resolution with no exposure to radiation. Flash UltraSound is also fast—it can capture a complete set of 3-D data of a breast for example, in a twentieth of a second, and process the data into an image in less than four seconds.

"We believe that Flash UltraSound has the potential to improve care and reduce costs through the earlier diagnosis of some of the most common types of cancer," says Geoff Bennett, InnerVision's chief operating officer.

Since establishing the company in 2002, the InnerVision team have been working hard on a number Tim Davies and Richard Evans saw an opportunity—a way
to dramatically improve ultrasound imaging, making it
faster and more accurate. Their acoustic-based technology
holds the promise of affordable disease screening. Their
innovation is now the core science behind Calgary-based
InnerVision Medical Technologies Inc. The privately
held company is engaged in the research, development, and
eventual distribution of ultra-high-resolution ultrasound
technology. Initial applications include the early detection
of breast and prostate cancer.

"Servicement with the TS Program has made use a better company" of fronts. They have developed an advanced prototype, proving the speed of Flash UltraSound and the economics of the technology. In the area of intellectual property protection, they filed a

US patent application in September 2004. Now the executive team is busy developing InnerVision's business strategy. To help with these activities, InnerVision applied for funding from AHFMR's Technology Commercialization (TC) Program. The money has been put to use in all these areas.

"We have gained considerable credibility from our association with AHFMR. A well-known independent organization has done its due diligence and funded us," notes Bennett. "We now have a greater chance of success with other funding agencies. It seems that no one wants to go first. The fact that AHFMR did makes it easier for others."

While InnerVision expected the credibility boost from the TC funding, there was also an unexpected outcome. "Involvement with the TC Program has made us a better company," says Bennett. "The AHFMR process was evidence-based. For them, everything was 'show me'. We knew what we were doing, but we hadn't yet developed a process of documentation and a style for communicating with the rest of the world. AHFMR forced us to accelerate those things."

Work is now underway on the design and development of a pre-commercial prototype, as well as market research and intelligence. Bennett describes InnerVision as being in transition: "We're moving from being a research-centric organization to being a commercially-oriented science company. It's a transition we must make, and the TC funding from AHFMR is helping us along."

THE SOURCE OF

seizures

Life can be difficult for the approximately 330,000 Canadians with epilepsy. These people must deal not only with the seizure disorder and its effects, but with the myths surrounding epilepsy and the stigma associated with it.

ife with epilepsy is especially difficult for the 5% to 10% of individuals with epilepsy who have trouble controlling their seizures with prescription drugs. These people can't drive and typically have difficulty working. They often need to take several medications; but the more drugs they use, the more likely they are to suffer side effects and problems arising from drug interactions.

Heritage Clinical Investigator Dr. Paolo Federico, who sees epilepsy patients at Foothills Medical Centre in Calgary, wants to find ways to improve life for individuals with uncontrollable seizures.

"We see these patients repeatedly," explains Dr. Federico, "When they have seizures they come into the emergency department. We adjust their medicines, and they might spend a day or two in hospital. They'll leave, but they come back a few weeks or months later. It's tough for them. That's why we're trying to find ways to help some of these individuals."

Dr. Federico leads a research team investigating where and how seizures are generated in the brain.

In some instances, neurologists are able to identify a specific brain site that generates the seizure. "Sometimes we can remove part of the brain in the hope of curing the patient's seizures. But sometimes these patients keep on having seizures despite removing the brain site from which seizures are presumably originating," explains Dr. Federico. "Perhaps seizures don't come from just one part of the brain. In some patients they might come from more diffuse networks that involve the surface and

deeper structures of the brain. There might be widespread circuits that underlie the generation of seizures."

Dr. Federico and his colleagues at the Seaman Family Magnetic Resonance Research Centre investigate better ways for surgeons to identify where to operate in patients with uncontrollable seizures. They use metic resonance imaging (MRI) to look at the

magnetic resonance imaging (MRI) to look at the networks in the brain that may be generating seizures; and they investigate blood flow changes related to brief seizures using a specific technique called functional MRI (fMRI). The research team has

"Perhaps seizures don't come from just one part of the brain."

Dr. Federico uses MRI to look at the networks in the brain

recently acquired equipment that allows them to use fMRI to look at seizures.

"This is a very sophisticated technique," explains Dr. Federico. "We record an electroencephalogram (EEG)—a record of the patient's brain activity—while the patient is lying in the tube of the MRI scanner. That's a technical feat in itself, because the scanner uses a high-field magnet that generates a lot of EEG artifact (unwinted electrical noise that obscures the recordings of brain activity). But the new equipment allows us to eliminate this noise. Using this technique, we have identified—in the small number of patients that we've recruited so far (about 20)—that there are diffuse networks in the brain, both on the surface and in deep structures, just as we hypothesized. We're changing the way scientists think about how seizures are generated."

Dr. Federico hopes that his research will help to better identify the epilepsy patients for whom surgery will be successful. "It's exciting," he says. "Right now the only benefit we can give them is to say that they're not good candidates for surgery and perhaps they should pursue other avenues of treatment."

Dr Paolo Federico is a Heritage Chinical Investigator and an assistant professor in the Department of Chinical Neurosciences, part of the Faculty of Medicine at the University of Calgary. He also receives a Canadian Institutes of Health Research (CIHR) operating grant for his research.

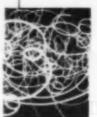
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Federico P, Briellmann RS, Abbott DF, Jackson GD. Functional MRI analysis of the pre-ictal state. Brain 2005. In press 2005.



Epilepsy: more common than you may know



According to statistics,
approximately 1% of the
Canadian population suffers
from epilepsy. But many with
the disorder are reluctant to
admit it or to seek treatment
due to the stigma surrounding
epilepsy and the prejudice with

which society has historically treated people with epilepsy. Thus, the prevalence of epilepsy is likely much higher than the statistics show.

Epilepsy is a neurological disorder, not a disease; it is not contagious. It is a serious physical disorder that affects one of the most vital parts of the body—the brain, which controls all our actions and emotions. Epileptic seizures result from the occasional malfunctioning of the brain. About 1% of all children will have recurrent seizures before age 14.

Seizures can take many different forms, including lapses of awareness, episodic shaking, or convulsions. Seizures usually don't last very long, normally only a minute or two, and then subside. In a few instances, doctors can trace seizures to specific causes, such as head injury from a car accident, the aftermath of a serious infection such as meningitis, or even lead poisoning, but most of the time we don't know why epilepsy occurs.

Each year, an average of 15,500 people in Canada learn that they have epilepsy—that's an average of 42 people each day.

- 44% are diagnosed before the age of 5
- . 55% before the age of 10
- 75 to 85% before the age of 18
- 13% of those diagnosed are over the age of 60

Source: Epilepsy Canada

ARTHORE: RICHARD MALLICAY.CONSTILLATION SERIES JUDG OF BIL STICK AND ACTIVITE ON CANADA BE S 68IN 1889 COURTESY OF THE ALBERTA FOUNDATION FOR THE ABIS.

LEFT: DR. PAOLO FEDERICO

The road to science

Bucharest to Edmonton. AHFMR Student Mircea Fagarasanu has travelled a long way on the road to becoming a scientist. He completed a medical degree in his native country of Romania, and while practising medicine, he discovered his passion for research.

anada seemed the "most friendly" of the countries in which Mircea considered pursuing this passion. A reputation for great research didn't hurt either. "I heard a lot of things about the post-graduate university environment from other

Romanians coming here, and I got an idea of the high-performance, professional environment," says Mircea. Although he was accepted to several universities across Canada, he chose the Faculty of Rehabilitation Medicine at the University of

Alberta because he could enter directly into the Ph.D. program, and because the faculty is "one of the best in North America in this field."

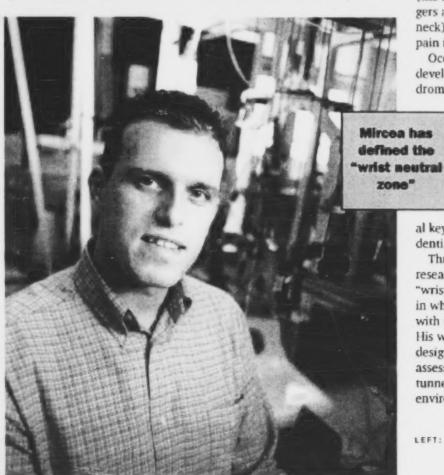
Mircea's research centres on occupational carpal tunnel syndrome, which he describes as the most commonly encountered nervous disorder of the upper extremities of the body. The condition occurs when the tendons in an area of the wrist called the carpal tunnel become swollen and put pressure on the median (the nerve running from the fingers all the way up the arm to the neck). This leads to tingling and pain in the hands and fingers.

Occupational risk factors for developing carpal tunnel syndrome include repetitive wrist

movement involving the application of force, and the maintenance of an awkward wrist position. Among the high-risk jobs for developing the disorder are office work using convention-

al keyboards, meat-cutting, and dentistry.

Through his multi-faceted research, Mircea has defined the "wrist neutral zone", the position in which the wrist is maintained with the lowest muscle activity. His work is also geared toward designing a better keyboard and assessing the prevalence of carpal tunnel syndrome in an office environment. He's keen to see



LEFT: MIRCEA FAGARASANU



his research applied to the workplace: "What's most important is returning the data to the fielddata kept in a drawer is no good." Mircea recently com-

only three years in the programan accomplishment he acknowledges modestly, while admitting it took a lot of hard work, especially during his first year. "Almost no one knew I was here. I was very, very busy."

Asked for advice to new graduate students, Mircea stressed the importance of finding an area of research that interested him. His positive relationship with his supervisor, Dr. Shrawan Kumar, professor of rehabilitation medicine and neuroscience, has also helped. "He's more than a supervisor," says Mircea. "He's a friend and sometimes a boss. He knows when to have a sense of humour and when to be tough."

Time management is another essential. "At the beginning, you have everything to do, and it feels like you don't have time for half of it." Mircea finds balance in activities such as soccer and boxing.

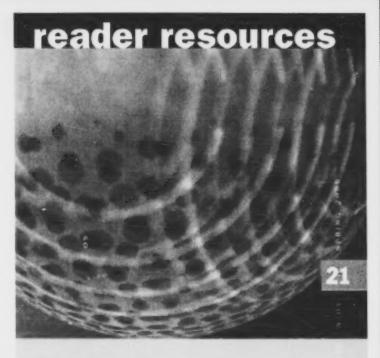
Mircea intends to stay in Edmonton. "At the beginning I didn't have roots here; now I have friends here. I have family." He is now working for the City of Edmonton as a corporate ergonomics consultant, where his research can help the organization stay productive while meeting worker-safety standards and reducing the risk of occupational health problems.

Mircea Fagarasanu is an AHFMR Fiealth Research Student who recently completed his Ph.D. in the Faculty of Rehabilitation Medicine at the University of Alberta. He has received an Alberta Provincial CIHR Training Program in Bone and Joint Health, a Mary Louise Imrie Graduate Student Award, an Honorary Izaak Walton Killam Memorial Scholarship from the University of Alberta, and a Meredith Graduate Fellowship from the Workers' Compensation Board.

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l'agarasanu M, Kumar S. Carpal tunnel syndrome due to keyboarding and mouse tasks: a review. International Journal of Industrial Ergonomics 2003 Feb;31(2):119-136.



Responding to the reader

University of Alberta Centre for Neuroscience http://www.neuroscience. ualberta.ca

Breathing problems in babies

The Association of Congonital Diaphragmatic Hernia Research, **Advocacy and Support** (CHERUBS) http://www.cherubs-CDH.org

Healthy schools, healthy choices

University of Calgary Centre for Health and Policy Studies http://www.chaps. ucalgary.ca

The details of life

Dr. Marie Frasor's website http://www.bio.ucalgary.ca /divisions/biochem/ fraser.html

The cancer puzzle

Alberta Cancer Board http://www.cancerboard. ab.ca

Canadian Cancer Society http://www.cancer.ca

Colorectal Cancer Screening Initiative Foundation http://www.ccsif.ca/ home.htm

National Cancer Institute of Canada

http://www.ncic.cancer.ca

The source of seizures

Epilepsy Canada http://www.epilepsy.ca

American Epilepsy Society http://www.aesnet.org

InnerVision

InnerVision Medical Technologies http://www.innermed.com

AHFMR announces \$40 million for health research

r. Brenda Hemmelgarn wants to find a better way to identify those with chronic kidney disease, and get them the specialized care and treatment they need early in the course of their illness. Her research addresses why certain groups of people, including the elderly and First Nations people. have a higher incidence of chronic kidney disease. She examines the differences between groups of people that may affect their access to treatment and care for this disease.

Dr. Hemmelgarn is one of 54 researchers around the province who was successful in AHFMR's 2005 senior personnel competition. She has been offered an award as a Population Health Investigator. This year AHFMR is offering \$40.7 million in grants to researchers at the universities of Alberta and Calgary. This year's competition includes successful applicants from a number of different university faculties including medicine; science; engineering: social work; arts; agriculture. forestry and home economics; and nursing. With the implemen-



tation of these awards, AHFMR will have contributed in excess of \$800 million to the medical research community in Alberta. For a complete list of AHFMR's 2005 senior personnel awards, go to: http://www.ahfmr.ab.ca

AHFMR 25th anniversary events

To mark AHFMR's 25th anniversary, the Foundation has planned a series of free lectures around the province on health research topics. Lectures planned for May will address the topic of pain and include the following dates and locations: May 4 - Edmonton Corbett Hall, University of Alberta

May 10 - Calgary Libin Theatre, University of Calgary

May 17 - Lloydminster Lakeland College

Lectures begin at 7:00 p.m.

For more information on these or other upcoming lectures, check AHFMR's website at http://www.ahfmr.ab.ca/25th_annive rsary or call AHFMR Communications at (780) 423-5727. Check back frequently for the details of health research lectures coming to a community near you in June.

Dear Reader,

If you are not already on our mailing list for our quarterly AHFMR Research News, and would like to receive it, please phone, fax, e-mail or write us and ask to be added to our subscribers list, it's free!

Phone: (780) 423-5727 and ask for AHFMR Communications

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Alberta Heritage Foundation for Medical Research 1500, 10104 - 103 Averue Edmonton, Alberta 151 4A7

ABOVE: DR. BRENDA HEMMELGARN WITH PATIENT

Physicians: please place in your patient waiting rooms.

